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GUARDANT HEALTH, INC.

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

GUARDANT HEALTH, INC.,
a Delaware corporation,

Plaintiff,

v.

NATERA, INC.,
a Delaware corporation,

Defendant.

Case No. 3:21-cv-04062-EMC

PLAINTIFF GUARDANT HEALTH, INC.'S MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF ITS MOTION FOR TEMPORARY RESTRAINING ORDER

Date: June 3, 2021
Time: 1:45 p.m. (Pacific Time)
Courtroom: Zoom Webinar

Complaint Filed: May 27, 2021

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Rules and Statutes

MEMORANDUM OF POINTS AND AUTHORITIES

I. INTRODUCTION

This case presents a textbook example where a restraining order should be granted under the Lanham Act. Plaintiff Guardant has just brought to market a cutting-edge diagnostic tool called Guardant Reveal™ ("Reveal") that can detect residual and recurrent colorectal cancer ("CRC") from a simple blood draw, with no need to sample or sequence tumor tissue. Defendant Natera sells a CRC assay called Signatera™ ("Signatera") using technology that requires tumor sampling and sequencing. Fearful that Guardant has developed a better assay posing a competitive threat to Signatera, and with the world's premier oncology research conference (the June 4-8 American Society of Clinical Oncology ("ASCO") 2021 Annual Meeting) fast approaching, Natera has cast aside the rules of fair competition and decided to play dirty. It has embarked on a scheme to squelch the successful launch of Reveal through an aggressive campaign of outright falsehoods, improper comparisons, and material misrepresentations regarding Reveal, which Natera has presented in complete disregard of the actual scientific evidence supporting Reveal's substantial benefits for cancer patients. Carefully timed to coincide with the launch of Reveal, including the critically important ASCO conference, Natera's false and misleading comparisons of Reveal and Signatera violate the Lanham Act and will continue to cause Guardant irreparable harm if not stopped.

Natera bases its false advertising on misleading apples-and-oranges characterizations of two separate studies—studies by different institutions, in different countries, with very different test protocols, analysis methods, and patient populations, and which in no way purport to reflect a head-to-head comparative analysis of Signatera and Reveal. In addition to creating the false impression that the studies provide an appropriate basis for comparison, Natera has made numerous false statements about specific metrics. These statements include:

- Misrepresenting that Signatera has a lower "failure rate" than Reveal (when in fact an apples-to-apples comparison would show the opposite).
- Touting Signatera's purportedly superior "pre-surgical sensitivity" when in fact Signatera cannot even be used as a pre-surgical diagnostic tool.
- Making a false and misleading comparison between 30-day post-surgical negative and positive predictive value data that falsely states the data for Reveal is "not reported" or "not validated" (and which relies on an inappropriate and misleading comparative metric in any

event).

- Making a false and misleading comparison regarding "diagnostic lead time" that lacks any reliable foundation.
- Making false, misleading, and unfounded comparisons regarding longitudinal negative predictive value data, hazard ratios, and sensitivity.

Because Guardant is likely to prevail on the merits of its § 43(a) Lanham Act false advertising claim, Guardant also presumptively has demonstrated irreparable harm for injunctive relief. 15 U.S.C. § 1116(a). Moreover, the threat of further irreparable harm to Guardant's reputation and customer good will is imminent. The nation's largest oncology professional's organization, ASCO, is holding its annual conference beginning this week, from June 4-8, and Natera will be there. *See* Decl. of Thereasa Rich, ¶¶ 38-39. Without an order restraining it from continuing its false advertising campaign, Natera will continue to "poison the well" against Reveal.[1] The Court therefore should issue a temporary restraining order and set a hearing for Guardant's application for preliminary injunction.

II. STATEMENT OF FACTS

Guardant draws this statement from the Declarations of Dr. Justin Odegaard, its Vice President, Clinical Development (and a pathologist and trained oncologist), and Ms. Rich, its Senior Medical Science Liaison ("Odegaard Decl." and "Rich Decl."), and exhibits attached thereto.

A. REVEAL, A PLASMA-ONLY ASSAY FOR COLORECTAL CANCER, OFFERS ONCOLOGISTS AND THEIR PATIENTS KEY ADVANTAGES

Guardant has a mission: To conquer cancer with data. Odegaard Decl. ¶ 2. A pioneer in non-invasive cancer diagnostics, Guardant was the first company to commercialize a comprehensive genomic liquid biopsy blood test that is used to profile and track tumor genomics and identify treatment options. Odegaard Decl. ¶ 10.

Unlike traditional tumor tissue biopsies, a liquid biopsy is non-invasive, and relies on a simple blood draw. *Id.* ¶ 13. Guardant's liquid biopsy assays detect fragments of DNA, called cell-

[1] The parties, through counsel, have conferred in an effort to avoid this Motion. Natera, however, has refused to refrain from relying on its advertising that has already been disseminated, and from continuing to make false and misleading comparisons of Signatera to Reveal in "unofficial" or "informal" presentations to or discussions with the parties' customers and potential customers, at ASCO or in the days before ASCO or after ASCO, necessitating judicial intervention.

free DNA (cfDNA) that are shed into the bloodstream by dying cells in tissues ("circulating tumor DNA," or "ctDNA"). *Id.* 13. Guardant's liquid biopsy assays are capable of detecting the presence of cancer in patients by detecting ctDNA in their blood without need of tumor tissue itself. *Id.*This makes it much easier to capture data about genomic alterations in an individual patient that emerge in response to treatment and over time, allowing for rapid and targeted therapies. *Id.* ¶ 4. Guardant's liquid biopsies represent a game-changing technology in the fight against cancer. *Id.* ¶ 13.

But Guardant is not about to rest on its laurels, and is committed to continuing its fight to help patients and oncologists address various cancers, including colorectal cancer (CRC). Thus, in additional to its gold-standard Guardant360, Guardant commercially launched the liquid biopsy-based Guardant360 CDx, and GuardantOMNI tests for advanced stage cancer patients, and recently launched Guardant Reveal™ for early-stage CRC patients. *Id.*

CRC is the third most commonly diagnosed cancer and the second leading cause of cancer death in the United States. *Id.* ¶ 11. While a majority of CRC patients are diagnosed with early-stage disease, nearly a third of patients whose CRC spreads into adjacent tissues and lymph nodes will die from their disease within five years. *Id.*

Surgery alone is often curative for early-stage CRC, and in later-stage cases, adjuvant chemotherapy after surgery can reduce the risk of recurrence. *Id.* ¶ 12. However, it is often unclear which patients need adjuvant chemotherapy, and many who receive it do so unnecessarily. *Id.* Until recently, clinicians have had very limited means of identifying patients that require adjuvant chemotherapy. *Id.* Thus, the development of effective clinical tests to identify CRC patients with Minimal Residual Disease (MRD)—i.e., a small number of CRC cells remaining in the body that can later multiply and cause recurrence of the disease—after surgery has long been recognized as a need, to help doctors both identify patients who may benefit from additional therapy and avoid administering unnecessary and toxic treatment to patients who will not benefit from it. *Id.*

But detecting and characterizing the very low concentrations of ctDNA present in the blood of CRC patients with MRD, and using that information to stratify patients as high- or low-risk for recurrence, requires an assay that is both highly sensitive and specific. Odegaard Decl. ¶ 14. To meet this challenge, Guardant expended substantial resources and time to develop Reveal, a clinical

blood-based assay to evaluate ctDNA in blood using advanced DNA sequencing methods. *Id.*

Reveal is the first commercially available plasma-only ctDNA assay, capable of detecting MRD in post-operative CRC patients in about seven days from a simple blood draw, without the need for prior sampling and sequencing of tumor tissue or the time needed to create a new, customized test for each new patient. Odegaard Decl. ¶¶ 15, 18. Reveal simultaneously interrogates genomic and epigenomic alterations. *Id.* ¶ 15. It accurately identifies genomic alterations down to allele frequencies of 0.01%, and effectively filters out biological noise sources such as mutations caused by clonal hematopoiesis that can lead to false positive results when testing for MRD. *Id.* The incorporation of biologically relevant epigenomic signatures is a key feature of Reveal that increases its test sensitivity in post-curative intent and surveillance indications. *Id.*

For oncologists, Reveal improves the management of early-stage CRC patients by detecting ctDNA in plasma after surgery, enabling doctors to identify patients with residual CRC who may benefit from post-surgery chemotherapy (adjuvant chemotherapy). Odegaard Decl. ¶¶ 15, 17. And as a liquid biopsy, Reveal offers major advantages for identifying MRD, because it is quick, convenient, and minimally invasive, and can be easily repeated to monitor for the presence of ctDNA over time. Odegaard Decl. ¶ 13; *see also* Rich Decl. ¶ 4.

Most importantly, Reveal works: Peer-reviewed data published by investigators at Massachusetts General Hospital ("MGH") in the journal *Clinical Cancer Research* (the "Parikh Study") shows that Reveal offers 91% recurrence sensitivity (*i.e.*, the ability to identify which patients will recur based on ctDNA detection) and 100% positive predictive value for recurrence (*i.e.*, all patients Reveal identified as having a "positive" ctDNA test result later recurred). Odegaard Decl. ¶ 16; *see also* Rich Decl. ¶ 32.

The Parikh Study was designed and led by investigators from MGH, the teaching hospital of Harvard Medical School, and not by Guardant (as Natera has falsely intimated). Rich Decl. ¶¶ 12-14. MGH issued a press release in April of 2021 underscoring MGH's leading role in the publication of the first ever data from a tumor-uninformed test for MRD. *See id.* ¶ 14 & Exhibit H thereto. The lead author, Aparna Parikh, MD, is an Assistant Professor of Medicine at Harvard Medical School, is a board-certified medical oncologist, is considered an expert in gastrointestinal

cancers, and liquid biopsies, and sits on the National Comprehensive Cancer Network (NCCN) guidelines committee for colorectal cancer—a set of guidelines widely used by oncologists in the U.S. *Id.* ¶ 12. She leads many clinical trials for patients with CRC and has co-authored over 50 publications. *Id.* She is also a paid consultant for Natera, but ***not*** Guardant. The study was co-authored by more than 30 other investigators at MGH who were involved in the preparation and review of all the data and analyses included in the Clinical Cancer Research publication. *Id.* ¶ 13.[2]

B. NATERA FALSELY ADVERTISES SIGNATERA AS SUPERIOR, CLAIMING REVEAL IS UNVALIDATED, UNTESTED, INACCURATE, AND INSENSITIVE

Natera markets and sells Signatera, which it describes as a "personalized, tumor-informed assay optimized to detect circulating tumor DNA (ctDNA) for molecular residual disease (MRD) assessment and recurrence monitoring for patients previously diagnosed with cancer." Rich Decl. ¶ 5. Signatera competes with Reveal in the market for ctDNA assays that can be used after surgery on CRC patients to detect recurrences and evaluate the need for adjuvant chemotherapy. *Id.* Unlike Reveal, Signatera is a tumor-dependent assay. *Id.*; *see also* Odegaard Decl. ¶ 17. It requires initial genomic profiling of tumor tissue taken from the individual patient. Information from the tumor tissue is then used to identify a panel of tumor-derived mutations specific to that patient, which then can be monitored through testing of blood samples collected throughout the patient's disease course. Odegaard Decl. ¶ 17.

Tumor-dependent assays like Signatera have drawbacks. Odegaard Decl. ¶ 18. Specifically, CRC patients—particularly those treated with chemotherapy prior to surgery—may not have sufficient samples of tumor tissue to allow initial genomic profiling of the tumor. *Id.*[3] For these

[2] The study's senior author, Ryan Corcoran, received his M.D. and a Ph.D in Cancer Biology from the Stanford University School of Medicine. Rich Decl. ¶ 13. He is a board-certified medical oncologist, Associate Professor at Harvard Medical School, the director of MGH's Gastrointestinal Cancer Center Program, and Principal Investigator of a translational research laboratory focused on personalized cancer medicine. *Id.* Dr. Corcoran is widely seen as an expert in gastrointestinal cancers and liquid biopsies, has co-authored more than six dozen publications including the NCI Colon and Rectal-Anal Task Force's whitepaper on ctDNA applications and integration in colorectal cancer, and has received consulting fees for his expertise from both Guardant and Natera. *Id.*

[3] This can occur in early stage cancers when patients have received neoadjuvant chemotherapy, which can kill the tumor in tissue samples, and when tissue samples are either unavailable due to logistical

patients, Reveal (a plasma-only ctDNA assay) provides the ***only*** option for MRD detection using ctDNA. *Id.* Without Reveal, these patients would be deprived of early recurrence detection and would be consigned to the traditional clinical risk stratification, which may result in over- or under-treatment. *Id.* ¶ 19. Even if sufficient tissue is available, the need to profile the tissue and develop an individualized array of assays can create significant delays in initial MRD testing turnaround time. *Id.* ¶ 18. Reveal obviates the dependency on tissue and reduces the time to attain results needed to decide whether high-risk patients require adjuvant chemotherapy ***from approximately three weeks to just 7 days***. *Id.* "For patients with a potentially lethal disease like CRC, this timely therapy decision-making is critical for both outcomes and peace of mind." *Id.*

Reveal addresses the real-world shortcomings of tumor-dependent assays like Signatera. Natera recognized this competitive threat and, beginning with the Reveal's launch, has undertaken an increasingly aggressive and deceptive campaign of misinformation to convince customers and potential customers, including oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, and genetic laboratories, to avoid using Reveal in favor of Signatera. In its commercial advertising and promotion, Natera makes literally false and misleading statements that disparage Guardant's new assay as unsupported by "peer-reviewed evidence," and falsely asserts that Signatera is superior to Reveal across a variety of metrics, including ***sensitivity***, ***failure rate***, ***negative predictive value (NPV)***, and ***hazard ratio***.[4] These claims are false. Natera combines outright misrepresentations with scientifically unfounded comparisons based on cherry-picked metrics, data artifacts, and non-comparable clinical studies to

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reasons (e.g. patient referred from another facility) or inadequate in either quantity or quality for follow-on MRD testing. Odegaard Decl. ¶ 19.

[4] "Sensitivity" refers to the assay's ability to identify which patients will develop recurrences based on MRD detection by ctDNA assay. A higher percentage indicates a test is more sensitive. "Failure rate" refers to the percentage of time a ctDNA assay fails to provide a result at all, whether positive or negative. For any test, a lower failure rate is more desirable. "NPV" refers to the assay's ability to correctly predict which patients will subsequently not develop a recurrence of CRC (i.e., a "negative" test result means CRC will not recur). The "Hazard Ratio" refers to a comparison between the recurrence rate over time in CRC patients who tested positive for MRD by ctDNA assay, to the recurrence rate in CRC patients who tested negative for MRD by ctDNA. A larger hazard ratio suggests that the assay is potentially more useful in successfully distinguishing CRC patients whose cancers will or will not recur. Rich Decl. ¶¶ 25.

exaggerate the purported benefits of Signatera while inaccurately denigrating Reveal. In truth, Reveal has important clinical advantages over Signatera—including its lower failure rate, superior landmark sensitivity, its availability for patients from whom tumor samples are unavailable, and its faster initial turnaround time from sample collection to assay results—all of which Natera conceals.

1. False Representations About Absence of "Peer-Reviewed Evidence"

Shortly after Reveal's commercial launch in February 2021, Natera began contacting current and potential customers, including leading cancer centers like the Mayo Clinic, expressing supposed "concern" about "other laboratories rushing into the clinical MRD market" and falsely suggesting that such other "laboratories" (*i.e.*, Guardant) were "making potentially misleading claims ***with no peer-reviewed evidence***, which may be detrimental to patients." In a promotional email dated March 2, 2021, which, on information and belief, Natera widely emailed to both its and Guardant's customers and potential customers, Natera stated:

> Natera is committed to the science and precision of molecular residual disease (MRD) testing for improving patient care. We are proud that Signatera data has been published or presented from over 2,000 patients across 30+ tumor histologies. As this exciting field gains momentum, especially in early-stage CRC, there is concern about other laboratories rushing into the clinical MRD market and making potentially misleading claims with no peer-reviewed evidence, which may be detrimental to patients. As you review the evidence for any new MRD test, please keep in mind several minimum requirements for MRD product performance and clinical validation.

Rich Decl. Exhibit B (emphasis in original). This statement is targeted at Guardant's new Reveal assay. The statement that "other laboratories" making "potentially misleading claims with no peer-reviewed evidence" is aimed directly at Guardant. Rich Decl. ¶ 6.

In the same promotional email, Natera sent these customers and potential customers a slide presentation entitled "Evidence Review: Tumor-informed vs. tumor-naïve MRD." Though again not identifying Reveal by name, Natera's presentation expressly references data presented by the Parikh Study authors at the 2020 European Society for Medical Oncology (ESMO) conference—a study specifically concerning Reveal. Moreover, Reveal is the only "tumor-naïve" (that is, plasma-only) ctDNA assay for detecting MRD in CRC patients available on the market, and is also the only ctDNA assay for MRD introduced at or around the time Natera sent this presentation. As with the statement in the March 2, 2021 email, Natera's "Evidence Review" characterizes "tumor-naïve

methods" (*i.e.*, Reveal) as unsupported by "peer-reviewed evidence." Rich Decl. ¶ 6 & Exhibit B.

Natera's repeated assertion that Reveal is unsupported by "peer-reviewed evidence" is false. In fact, interim data from the very study cited by Natera—the Parikh Study—***was peer-reviewed before being published***, first as abstract-presentations at three separate prestigious scientific meetings (ASCO 2019, ESMO 2019, and ESMO 2020), and later as an article in the April 29, 2021 issue of the journal *Clinical Cancer Research*. Rich Decl. ¶ 7 & Exhibits C-E & J.

2. Misleading Comparisons and False Statements About Comparative Metrics

Any valid comparison between diagnostic tests, including ctDNA assays—and specifically including Signatera and Reveal—must be supported by properly designed, head-to-head studies that directly compare the two assays using the same test procedures and protocols in the same patient population. Odegaard Decl. ¶ 20; see also Rich Decl. ¶ 16. Cross-test comparisons, especially where the purpose and methodology of the underlying studies differ significantly, and/or where the studies are conducted in different patient populations, necessarily lead to a misleading apples-to-oranges result that cannot legitimately be used to claim that one test is superior to the other. *Id.*; *see also* Rich Decl. ¶ 16.

To date, no such head-to-head studies involving Signatera and Reveal and using the same test protocol and study population are available. Odegaard Decl. ¶ 21. Natera, however, has published purported "performance comparisons" of Signatera and Reveal that rely on data from ***different*** studies (the Parikh Study data concerning Reveal, and data published by Reinert et al. (the "Reinert Study") for Signatera). Odegaard Decl. ¶¶ 22-23; Rich Decl. ¶ 17. These studies were run in different countries, used very different test protocols and analysis methods, and examined very different patient populations. Rich Decl. ¶ 17 & 34-35. Thus, Natera's claims of superiority based on these improper comparisons are false, misleading, and deceptive. As set forth below, Natera compounds the misleading nature of these comparisons by making false and misleading statements about the purported "metrics" used in the comparisons to show Reveal's supposed inferiority.

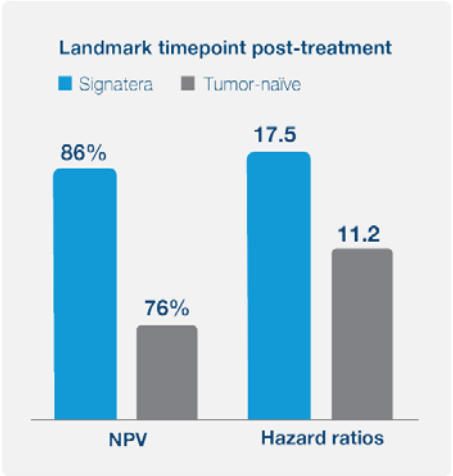
For example, in March 2021, Natera began publicly asserting that while Signatera's "test performance" is "unsurpassed," Reveal is not only inferior to Signatera, but has "unknown" performance with respect to sensitivity and hazard ratios for "time points" that "matter":

Three time points matter for performance assessment in CRC

	Signatera HR[1,3]	Tumor-naïve HR[2]
Single test 30 days post-surgery	7.2-14.0*	Unknown
Single test post-treatment	17.5	11.2
Serial testing in surveillance	43.5-47.5	Unknown

	Signatera NPV[1]	Tumor—naïve[2]
Single test 30 days post-surgery	88% (74/84)	Unknown
Single test post-treatment	86% (44/51)	76% (37/49)
Serial testing in surveillance	97% (58/60)	Unknown

*3/10 post-surgical positive patients cleared ctDNA with adjuvant chemotherapy and did not relapse, implying 70% PPV in patients who receive subsequent ACT



1. Reinert T, Henriksen TV, Christensen E, et al. Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. *JAMA Oncol*. 2019;5(8):1124–1131.
2. Parikh, A. et. al. Minimal residual disease (MRD) detection in colorectal cancer (CRC) using a plasma- only integrated genomic and epigenomic circulating tumor DNA (ctDNA) assay. ESMO 2020
3. Tarazona N, Henriksen T, Carbonell-Asins J, et al. Circulating tumor DNA to detect minimal residual disease, response to adjuvant therapy and identify patients at high risk of recurrence in stage I-III CRC. ASCO Poster. 2020

Rich Decl. Exhibit B.

Natera then published a purported "white paper" on its website for the express purpose of comparing "how our tumor-informed approach stacks up against a tumor naïve assay":

Table 3. *Comparison of hazard ratios and negative predictive values of tumor-informed and tumor-naive assays in early-stage CRC*

	Signatera (tumor-informed assay)[4,7,8]	Tumor-naive assay[19]
Hazard ratios of ctDNA (positive vs negative)		
Post-surgery (30 day single test)	7.2-14.0*	Not Validated
Post-ACT (single test)	17.5	9.8-11.2**
Serial testing	43.5-47.5	11.4
Negative predictive value (NPV)		
Post-surgery (30 day single test)	88% (74/84)	Not Validated
Post-ACT (single test)	86% (44/51)	76% (37/49)**
Serial testing	97% (58/60)	82% (41/50)

The "white paper" is still on Natera's website and can be found at https://www.natera.com/wp-content/uploads/2021/05/SGN_WP_Solar_20210503_NAT-9000052_FINAL_DWNLD.pdf. Rich Decl. Exhibit F. This misleading public document purports to compare "Signatera (tumor informed assay)" to a "Tumor-naïve assay" (*i.e.*, Reveal), citing data purporting to show that Reveal is "not

validated," or that Signatera significantly outperforms Reveal on every referenced metric, including "Hazard ratios" and "Negative predictive value (NPV)."

In the past month, Natera's false advertising has become even more aggressive, and more blatantly misleading. In May 2021, Natera published a false and misleading "Investor Presentation," which purports to compare "Signatera vs. Reveal performance":

Signatera vs. Reveal performance comparison

	Signatera	Reveal
Validation data published or presented (# patients analyzed)	> 2,000[1,2]	< 150[4,5]
Pre-surgical sensitivity in CRC	89-94%[1,3]	47%*[4]
Failure rate in CRC – tissue and plasma combined	< 3%[3]	12-14%[4]
Number of blood tubes required	2	4
Diagnostic lead time vs. radiographic recurrence in CRC (avg)	8.7 months[1]	~4 months*[4]
Post-surgical NPV/PPV in CRC (30 days post-surgery)	88% / 100%**[1]	not reported[4]
Serial longitudinal NPV in CRC	97%[1]	82%[4]
Serial longitudinal Hazard Ratio in CRC	43.5[1]	11.4[4]
Serial longitudinal sensitivity in CRC	88-94%[1,2]	69%[4]
Quantitation of ctDNA burden for monitoring purposes	Tumor copies per mL	none

Rich Decl. Exhibit G.

Shortly after posting the May 2021 performance comparison on its website, Natera began widely disseminating it—often repeatedly—to the same customers and potential customers to tout Signatera's supposed superiority over Reveal, and to disparage Reveal. Rich Decl. ¶ 10. Like its "Evidence Review" and white paper advertising, Natera's May 2021 performance comparison claims to demonstrate quantitatively that Signatera is superior to Reveal across a wide-ranging set of metrics, including "pre-surgical sensitivity," "failure rate," "diagnostic lead time,"[5] "post-surgical" and "serial longitudinal" negative predictive value (NPV), and "Hazard Ratio," among other categories. *Id.*

The comparisons listed above are false and misleading. Not only are cross-test "comparisons" based on different studies with different test protocols, different analysis methods,

[5] "Diagnostic lead time" refers to the time between the first MRD detection by ctDNA assay and the first confirmation of CRC recurrence by standard radiographic imaging methods. A longer diagnostic lead time is generally observed with higher sensitivity tests.

and different patient populations inherently misleading, but Natera's presentation of the specific individual "metrics" contains numerous misleading statements and outright falsehoods.

Failure rate: Natera's comparison of "failure rate in CRC," and its claims that Signatera has a lower failure rate than over Reveal, are false and misleading. As the article published by the Parikh Study authors in the April 29, 2021 issue of Clinical Cancer Research states, the Parikh Study—which Natera cites as proof that Reveal has a "12-14%" failure rate (vs. a "< 3%" rate for Signatera)—relied on ***banked*** plasma or cell free DNA samples that had input amounts substantially less than recommended. Indeed, as stated explicitly in April 29 article, "the extracted ctDNA quantity or quality was below the recommended and optimal input levels for the assay" and "may have affected overall performance characteristics." Rich Decl. ¶ 23.

Guardant's data show the actual failure rate of Reveal in patient care testing is less than 1%, better than Signatera's claimed failure rate of less than 3%. Rich Decl. ¶ 24. But even this comparison fails to account for the fact that while Reveal relies solely on plasma, a successful test using Signatera requires *both* plasma and usable tumor tissue samples. Odegaard Decl. ¶ 17. The rate of sample failure among submitted tissue samples in the U.S. is far higher than 3%. Rich Decl. ¶ 24. And, for many patients, a tumor tissue sample is unavailable. Odegaard Decl. ¶¶ 18-19. Natera's touted failure rate appears to omit this population, for whom Signatera is never an option.

Pre-surgical sensitivity: Natera's claims of Signatera's superior "pre-surgical sensitivity" ("89-94%" vs. "47%") is functionally meaningless and highly misleading. Reveal is not intended or indicated to be used as a diagnostic tool pre-surgery. Rich Decl. ¶ 30. And, as an assay that relies on the existence of surgically-excised tumor tissue, Odegaard Decl. ¶ 17, Signatera ***cannot*** be used as a ***pre***-surgical diagnostic tool. Rich Decl. ¶ 25. Thus, Natera's claim of "89-94%" pre-surgical sensitivity for Signatera is plainly misleading. *Id.* Moreover, the study Natera cites as the source of this statistic—the Parikh Study—contains a population where nearly half (45%) of the study cohort received chemotherapy prior to surgery and in which the pre-surgical sample volumes were far lower than recommended. *Id*. Such pre-surgical treatment suppresses ctDNA, and thus necessarily lowers the ctDNA detection rate. Low sample volume can likewise affect assay sensitivity. *Id.* Again, Natera has falsely depicted an apples-to-oranges comparison as an apples-to-apples

analysis, while falsely touting an intentionally skewed "metric" with no real-world significance. *Id.*

Post-surgical NPV/PPV: Natera's further comparison of the 30-day ***post***-surgical negative and positive predictive value (NPV/PPV) for Signatera vs. Reveal, (i.e., 88%/100% vs. "not reported" or "not validated"), is similarly misleading. Rich Decl. ¶ 8. For many CRC patients, surgery to remove the tumor does not represent the end of the patient's initial treatment regimen. Many patients receive adjuvant chemotherapy soon after surgery. *Id.* ¶ 27; *see also* Odegaard Decl. ¶ 12. While—contrary to Natera's claim—the Parikh Study authors did report data that could be used to calculate a 30-day post-surgical NPV and PPV for Reveal, the authors did not focus on—nor did they draw conclusions from—data from this timepoint. Rich Decl. ¶ 27.

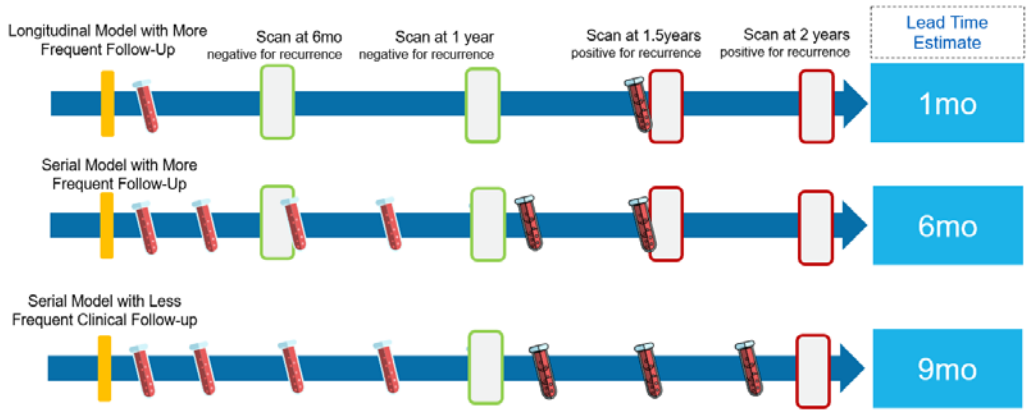
The 30-day post-surgical MRD timepoint is not the appropriate timepoint in an observational/retrospective research study to validate performance metrics, like PPV or NPV, of assays like Signatera or Reveal that are intended to predict disease recurrence. Rich Decl. ¶¶ 27-28. This is because, put simply, adjuvant therapy works, and can cure MRD-positive patients that otherwise would have recurred. *Id.* ¶ 28. As such, estimates of an assay's NPV and PPV, when sourced from samples collected ***after surgery but before adjuvant chemotherapy***, are confounded by the effect of chemotherapy and are uninterpretable—one cannot sort out the merits of the assay from the effects of the chemotherapy. *Id.* The Parikh Study authors purposely chose to report data from samples collected ***after all definitive treatment*** to avoid this confounding factor precisely because nearly 55% of the study participants received additional treatment post-surgery. *Id.*

On the other hand, sensitivity to detect recurrence is not subject to the confounding effect of post-operative chemotherapy. Rich Decl. ¶ 29. Nor is sensitivity subject to the confounding effects of the baseline population risk, as described below. *Id.* Thus sensitivity is a more appropriate metric to compare assay performance at the 30-day post-surgery timepoint than NPV. *Id*. However, Natera chose not to report this metric in its marketing materials, presumably because it shows Signatera's performance is *less* favorable compared to Reveal. *Id.* As reported in the Reinert Study, the sensitivity of Signatera to detect recurrence using the 30-day post-surgical timepoint is 7/17 patients (41%). *Id.* This metric as reported by the Parikh Study authors in the supplemental data shows 14/26 patients (54%). *Id.* Among the subset of patients with stage I-III disease (excluding

stage IV patients, who were not including in the Reinert Study), the Reveal data show an even higher sensitivity for recurrence of 9/16 (56%). *Id.*

In short, PPV as a metric of assay validity must be taken from samples collected after all therapy is complete and where sufficient follow-up is available. Underscoring the importance of this—and the misleading nature of the values presented by Natera's advertising—the PPV for both assays is **100%** when these conditions are met.

Diagnostic lead time: Natera's unfavorable comparison of Reveal's "diagnostic lead time vs. radiographic recurrence," to that of Signatera, is also false and misleading. The calculation of a "diagnostic lead time estimate" is affected as much by the frequency of the tests that are used to derive the estimate as it is by the assay's actual sensitivity. As the following graphic shows, the diagnostic lead time estimate for the ***same assay and the same patient with same test results*** can vary significantly, depending on how often follow-up testing is conducted. *See* Rich Decl. ¶ 33:



Because Natera's diagnostic lead time estimates are derived from studies having different protocols and testing regimens, its comparison is fundamentally flawed and unreliable. *Id.* The "diagnostic lead time estimate" for Signatera was developed from data reported by the Reinert Study authors. *Id.* ¶ 34. The Reinert Study's protocol called for CRC patients to undergo ctDNA testing 30 days after surgery, and every three months afterwards, for three years or until the patient's death or withdrawal from the study. The Reinert Study was also conducted in Denmark, where radiographic scans are relatively infrequent. Reinert reported radiographic scans were performed 12 months and 36 months after surgery. *Id.* Infrequent scans may have artificially inflated Signatera's supposed diagnostic lead time, particularly when applied to U.S. patients, where the

standard-of-care calls for more frequent scans. *Id.* ¶¶ 34-35 (noting NCCN guidelines recommend scans every 6-12 months after surgery). In contrast, the Parikh Study did not involve patient testing at regular intervals over a specified period of time and was not designed to estimate "diagnostic lead time." *Id.* Consequently, the Parikh Study authors did not report an estimated diagnostic lead time for Reveal, and the "~ 4 months" value Natera fabricated for Reveal has no reliable basis. *Id.*

"Serial longitudinal" NPV, hazard ratio, and sensitivity: Natera's comparisons of the "serial longitudinal" NPV, hazard ratio, and sensitivity of Signatera and Reveal are fundamentally misleading. Rich Decl. ¶ 31. Dr. Parikh did not design her study to provide "serial" test data (i.e. testing at regular time intervals after the initial test), and consequently did not report these statistics. *Id.* Natera nevertheless biased its comparison with Reveal in Signatera's favor by reporting the Parikh Study's "***longitudinal***" sensitivity of 69%, which is calculated in patients who had at least one surveillance draw, the timing of which was highly variable relative to the time of recurrence, and is in no way similar to the timing of sample collection employed in the Reinert Study. *Id.*

This is, once again, a fundamentally a misleading apples-to-oranges comparison. Making Natera's presentation even more inexcusable, the Parikh Study includes a subset of recurrence positive patients who had a Reveal sample available within 4 months of recurrence. *Id.* ¶ 32. Using *these* data to estimate the "***serial*** longitudinal" sensitivity parameter, Reveal has an estimated sensitivity of 91%—comparable (or superior) to Signatera. Despite the valid estimate of 91% being clearly outlined in the Parikh Study, Natera chose to use a fabricated and invalid "longitudinal" sensitivity estimate, again presumably because it cast Reveal in a less favorable light. *Id.*

Beyond its choice to disregard differences in testing frequency, Natera further biased its serial longitudinal NPV and hazard ratio comparisons by ignoring the significant differences in the patient populations from which the data were drawn. The Reinert Study using Signatera examined patients with a CRC recurrence rate of 19% (24/125 evaluable patients). Rich Decl. ¶ 26. In contrast, the patients included in the Parikh Study were more than twice as likely to recur (39%, 27/70 evaluable patients) demonstrating that the patients in this study had a much higher risk of disease recurrence than those in the Reinert Study. *Id.* Assays of equal sensitivity and specificity yield dramatically different NPVs and hazard ratios when applied to patient populations with

different risk profiles. *Id.* Natera's deliberate failure to account for this difference results in false and highly deceptive comparisons.

Natera's claim in the "Evidence Review" that "tumor-naïve" testing has "unknown" performance with respect to sensitivity and hazard ratios for a single test 30 days post-surgery is false. These data are not "unknown." In fact, they were presented in the ASCO 2019 abstract by Parikh et al, available well before Natera's dissemination of the Evidence Review. *Id.* ¶ 27.[6]

III. ARGUMENT

"The standard for issuing a TRO is identical to the standard for a preliminary injunction." *Cisco Sys., Inc. v. Shenzhen Usource Tech. Co.*, No. 5:20-cv-4773, 2020 WL 5199434, at *6 (N.D. Cal. Aug. 17, 2020) (issuing TRO enjoining defendants from violating Lanham Act) (citing *Stuhlbarg Int'l Sales Co., Inc. v. John D. Brush & Co.*, 240 F.3d 832, 839 n.7 (9th Cir. 2001); *Lockheed Missile & Space Co. v. Hughes Aircraft,* 887 F. Supp. 1320, 1323 (N.D. Cal. 1995)). "A plaintiff seeking preliminary injunctive relief must establish that":

(1) it is likely to succeed on the merits;
(2) it is likely to suffer irreparable harm in the absence of preliminary relief;
(3) the balance of equities tips in his favor; and
(4) an injunction is in the public interest.

Id. (quoting *Winter v. Natural Res. Defense Council, Inc.*, 555 U.S. 7, 20 (2008)). Moreover, under the Ninth Circuit's "sliding scale" approach, "'if a plaintiff can only show that there are serious questions going to the merits—a lesser showing than likelihood of success on the merits—then a preliminary injunction may still issue if the balance of hardships tips *sharply* in the plaintiff's favor, and the other two *Winter* factors are satisfied.'" *Id.* (citations omitted).

This Court "enjoy[s] considerable discretion in determining whether an injunction should issue and in formulating its terms." *Taylor by and Through Taylor v. Honig,* 910 F.2d 627, 631 (9th Cir. 1990). While the standards for TROs and temporary injunctions are the same, "[d]ue to the urgency of obtaining a preliminary injunction at a point when there has been limited factual development, the rules of evidence do not apply strictly to preliminary injunction proceedings."

[6] In addition to these core falsehoods, Natera falsely touts Signatera as being superior to Reveal on metrics that have no relationship to the accuracy of an assay. Rich Decl. ¶¶ 20-22.

Herb Reed Enters., LLC v. Florida Ent. Mgmt., Inc., 736 F.3d 1239, 1250 n.5 (9th Cir. 2013).

A. GUARDANT IS LIKELY TO SUCCEED ON THE MERITS

"[T]he Lanham Act is at heart a consumer protection statute." *TrafficSchool.com, Inc. v. Edriver Inc.*, 653 F.3d 820, 827 (9th Cir. 2011). Here, "'[t]he great evil the Lanham Act seeks to prevent,'" *id.*, includes the lost time and lost opportunities for patients and their doctors fighting cancer, when Natera's false and misleading attacks on Reveal lead oncologists to reject an extremely sensitive, reliable, fast assay that, for some patients, is the only ctDNA option to predict the recurrence of their potentially fatal CRC.

Section 43(a) of the Lanham Act, 15 U.S.C. § 1125(a), allows an action against "[a]ny person who," in connection with goods or services, uses in commerce "any word" or "misleading description of fact" which "in commercial advertising or promotion, misrepresents the nature, characteristics, qualities, or geographic origin of his or her or another person's goods, services, or commercial activities[.]" The claim's elements are:

(1) the ads of the opposing party were false or misleading;
(2) the ads deceived, or had the capacity to deceive, consumers;
(3) the deception had a material effect on purchasing decisions;
(4) the misrepresented product affects interstate commerce; and
(5) the claimant has been, or is likely to be, injured by the false advertising.

Southland Sod Farms v. Stover Seed Co., 108 F.3d 1134, 1139 (9th Cir. 1997); *see also Clorox Co. v. Reckitt Benckiser Grp. PLC*, 398 F. Supp. 3d 623, 635 (N.D. Cal. 2019).

Advertising includes any communications made in connection with the sale of goods. *Williams v. Gerber Prods. Co.*, 552 F.3d 934, 939 (9th Cir. 2008). Advertising "is not limited to newspaper, television or radio announcements; any notice *addressed to the public* serves the same purpose." *Hyosung Am., Inc. v. Sumagh Textile Co., Ltd.*, 934 F. Supp. 570, 580 (S.D.N.Y. 1996), *aff'd in part, rev'd in part on other grounds*, 137 F.3d 75 (2d Cir. 1998). Thus, secondary distribution of medical journal articles is "advertising." *Bracco Diagnostics, Inc. v. Amersham Health, Inc.*, 627 F. Supp. 2d 384, 459 (D.N.J. 2009).

B. NATERA'S ADVERTISING IS LITERALLY FALSE

Natera's advertising is actionable if it is (1) literally false or (2) literally true, but likely to mislead or confuse consumers. *Southland Sod*, 108 F.3d at 1139, *Clorox*, 398 F. Supp. 3d at 635.

When a statement is literally false, the court presumes deception. *U-Haul Int'l, Inc. v. Jartran, Inc.*, 793 F. 2d 1034, 1040-41 (9th Cir. 1986). A "literally false" message may be explicit or "conveyed by necessary implication when, considering the advertisement in its entirety, the audience would recognize the claim as readily as if it had been explicitly stated." *Novartis Consumer Health, Inc. v. Johnson & Johnson-Merck Consumer Pharm. Co.*, 290 F.3d 578, 586-87 (3d Cir. 2002).

Advertising claims of product superiority based on testing are false if the "tests 'are not sufficiently reliable to permit one to conclude with reasonable certainty that they established' the claim made." *Southland Sod*, 108 F.3d at 1139 (citations omitted). "A plaintiff may meet this burden either by attacking the validity of the defendant's tests directly or by showing that the defendant's tests are contradicted or unsupported by other scientific tests." *Id.* Such establishment claims also "may be proven false by showing that the tests did not establish the proposition for which they were cited." *Id.* (construing *Castrol, Inc. v. Quaker State Corp.*, 977 F.2d 57, 62-63 (2d Cir. 1992)). Thus, "if the plaintiff can show that the tests, even if reliable, do not establish the proposition asserted by the defendant, the plaintiff has obviously met its burden of demonstrating literal falsity." *Id.* (quotations omitted); *see also Novartis*, 290 F.3d at 590 ("a completely unsubstantiated advertising claim by the defendant is *per se* false without additional evidence from the plaintiff to that effect"); *Osmose, Inc. v. Viance, LLC*, 612 F.3d 1298, 1309 (11th Cir. 2010) ("In order to prove the literal falsity of such [an establishment] claim, the plaintiff must prove only that the tests did not establish the proposition for which they were cited.")

1. Natera's Comparative Claims Are Literally False

Each and every statement challenged in this motion is literally false. Natera has not performed a study directly comparing Signatera and Reveal. "[I]t is a fundamental principle of clinical testing that one cannot infer efficacy comparisons between two products when, as here, those products have not been tested against one another in a well-controlled head-to-head clinical study." *Zeneca Inc. v. Eli Lilly and Co.,* No. 99-cv-1452, 1999 WL 509471, at *35 (S.D.N.Y. Jul. 19, 1999); *see also CareDx v. Natera, Inc.,* No. 19-cv-662, 2020 WL 401773, at *1 (D. Del. Jan. 24, 2020) (denying motion to dismiss where "[t]he thrust of the Complaint is that Natera falsely and misleadingly suggested that the relevant studies show that Natera's product was superior to

CareDx's product when in fact . . . the studies are not head-to-head studies that would support comparisons of the two competing products."); *Healthport Corp. v. Tanita Corp. of Am.*, 563 F. Supp. 2d 1169, 1174, 1179 (D. Ore. 2008) (permanently enjoining counter-defendant from falsely advertising its product as being "unequaled in accuracy and validity as compared to other body composition analyzers" because "Healthport's principals testified they did no comparative or tests to verify" these claims) (citing *Southland Sod Farms*, 108 F.3d at 1139)); *Church & Dwight Co. v. S.C. Johnson & Son, Inc.*, 873 F. Supp. 893, 905-06 (D.N.J. 1994) (permanently enjoining comparative ads as literally false where defendant "never performed head-to-head studies comparing the efficacy" of compared products); *Thompson Medical Co., Inc. v. Ciba-Geigy Corp.*, 643 F. Supp. 1190, 1195 (S.D.N.Y. 1986) (enjoining comparative advertising claims "of therapeutic advantage or superiority" of competing appetite suppressant "unless and until plaintiff has at least one adequate and well-controlled comparative clinical study which demonstrates such therapeutic advantage or superiority").

As set forth above, and as further described in Dr. Odegaard's and Ms. Rich's declarations, each of Natera's promotional claims of quantitative superiority, including the express and implied claims contained in its "Evidence Review," "white paper," and the "Signatera vs. Reveal performance comparison," are based on the false and misleading premise that a reliable head-to-head study actually exists. *See CareDx*, 2020 WL 401773, at *1. Because no such study exists, all of Natera's statements comparing Signatera to Reveal discussed above are literally false.

Further, as detailed above, Natera has also made false and misleading statements regarding the individual metrics depicted in the purported "comparisons." Natera has, among other things:

- Misrepresented that Signatera has a lower "failure rate";
- Falsely touted Signatera's purportedly superior "pre-surgical sensitivity";
- Made a false and misleading comparison between 30-day post-surgical negative and positive predictive value data that falsely states the data for Reveal is "not reported" or "not validated"; and
- Made a false and misleading comparison regarding "diagnostic lead time."

These statements are literally false and create a highly misleading impressions about Signatera's purported comparative advantages over Reveal—"advantages" that are wholly unsupportable from

the underlying data. These statements have deceived, and are highly likely to deceive, oncologists and other physicians, cancer researchers, health care institutions, biopharmaceutical companies, and genetic laboratories, and other customers and potential customers into believing that Reveal is untested, inaccurate, insensitive, and inferior to Signatera, to their own detriment and to the detriment of patients who may not have the opportunity to use Reveal because of the misstatements.

2. Natera's False Advertising Is Deceptive And Material

Literally false advertising creates a presumption of consumer deception. *Avid Identification Sys., Inc. v. Schering-Plough Corp.*, 33 Fed. App'x 854, 856 (9th Cir. 2002) (citing *William H. Morris Co. v. Group W, Inc.*, 66 F.3d 255, 258 (9th Cir. 1995)). "The expenditure by a competitor of substantial funds in an effort to deceive consumers and influence their purchasing decisions justifies the existence of a presumption that consumers are, in fact, being deceived." *U-Haul*, 793 F.2d at 1041. Thus, "[h]e who has attempted to deceive should not complain when required to bear the burden of rebutting a presumption that he succeeded." *Id.*; *Harper House, Inc. v. Thomas Nelson, Inc.*, 889 F.2d 197, 209 (9th Cir. 1989) (applying *U-Haul* to find presumption of deception and injury); *Soaring Helmet Corp. v. Nanal, Inc.*, No. C:09-cv-0789, 2011 WL 39058, at *6 (W.D. Wash. Jan. 3, 2011) ("a finding that the advertisement was literally or facially false leads to a presumption of consumer deception and materiality in a false advertisement case").

A misrepresentation as to an inherent characteristic of the product sold is clearly "material." *POM Wonderful LLC v. Purely Juice, Inc.*, No. 2:07-cv-02633, 2008 WL 4222045, at *11 (C.D. Cal. July 17, 2008) ("[t]he fact that [defendant's] false advertising pertained to the very nature of its juice product establishes its materiality."), *aff'd*, 362 Fed. App'x 577 (9th Cir. 2009). The qualities and characteristics of medical products are by definition material. *See*, *e.g.*, *North Am. Med. Corp. v. Axiom Worldwide, Inc.*, 522 F.3d 1211, 1226 (11th Cir. 2008) (false representations regarding physiotherapeutic spinal device "logically would influence a doctor's decision to purchase the DRX 9000 over a competing machine without those qualities").

Natera's literally false advertising, both about Signatera's supposed superiority and Reveal's alleged failings, are plainly material. All of the misleading statements are directed toward the accuracy and reliability of Reveal – critical considerations for any diagnostic tool.

The Court may also presume Natera's literally false advertising is material. *Sinai v. Bureau of Auto. Repair*, 28 U.S.P.Q.2d 1627, 1993 WL 341276, at *2 (N.D. Cal. Sept. 1, 1993) ("explicitly false statements are presumed material"); *Align Tech., Inc. v. OrthoClear, Inc.*, No. 3:05-cv-02948-MMC, 2006 WL 2374608, at *1 (N.D. Cal. Aug. 16, 2006) ("where defendant deliberately makes false statement, trier of fact entitled to presume false statement deceived consumers and was material."); *accord, Cochran Firm, P.C. v. Cochran Firm L.A. LLP*, No. 2:12-cv-05868, 2016 WL 6023822, at *6 (C.D. Cal. Aug. 18, 2016) (literally or deliberately false statements create a presumption of deception and reliance).

Finally, to the extent any of the challenged statements can be described as "literally true" (which they are not), they are still actionable if they are "likely to mislead or confuse consumers." *Southland Sod*, 108 F.3d at 1139. For the reasons set forth above, the challenged statements are misleading. Because they purport to represent results of comparative studies with respect to metrics purporting to bear on accuracy and reliability, they are precisely the sort of statements that are "likely to mislead or confuse consumers."

3. Guardant Has Been Injured By Natera's Literally False Advertising, and The Products Affect Interstate Commerce

"[A] competitor need not prove injury when suing to enjoin conduct that violates section 43(a)." *Harper House*, 889 F.2d at 210. Here, Natera's statements are precisely the sort of material misrepresentations that are likely to dampen demand for a newly marketed product like Reveal. Natera's express and necessarily implied assertions that Reveal has "significant gaps in study design and performance," and is less sensitive and predictive than Signatera, sow doubt among oncologists and others about the utility and performance of Reveal. Natera explicitly reinforces this doubt by warning doctors that using Reveal may 'be detrimental to patients." Natera's assertions will cause, and on information and belief may have already caused, some CRC patients to lose opportunities for rapid MRD detection and the attendant benefits of timely guided treatment decisions.

Natera's statements are in interstate commerce, Rich Decl. ¶ 4, and have already reached numerous oncology professionals. And the false and disparaging advertising is having the effect

Natera intended. For example, a biopharma company that had been shown the Natera-authored comparison chart that makes false and misleading assertions about Reveal contacted Guardant, and called on Guardant to "stand and defend" Natera's claims. Odegaard Decl. ¶ 28.

Given that Natera's advertising will likely reach thousands of oncology professionals this weekend if Natera is allowed to continue making false and misleading statements at ASCO, the evidence and common sense support a high likelihood of significant injury if it is not immediately enjoined, including substantial and wholly unwarranted reputational damage.

Guardant has presented substantial evidence meeting all the elements of a § 43(a) Lanham Act false advertising claim, and is likely to prevail on this claim at trial. At the very least, Guardant presents "serious questions going to the merits" of the claim, permitting the grant of temporary injunctive relief. *Alliance for the Wild Rockies v. Pena*, 865 F.3d 1211, 1217 (9th Cir. 2017).

C. GUARDANT WILL CONTINUE TO SUFFER IRREPARABLE HARM IF NATERA IS NOT ENJOINED

Lanham Act claims are particularly well-suited for injunctive remedies. Not only does the Lanham Act expressly provide for injunctive relief, but Congress amended the statute to create a *presumption* or irreparable harm where the movant shows a likelihood of success on the merits:

> ***A plaintiff seeking any such injunction shall be entitled to a rebuttable presumption of irreparable harm*** upon a finding of a violation identified in this subsection in the case of a motion for a permanent injunction or upon a finding of likelihood of success on the merits for a violation identified in this subsection in the case of a motion for a preliminary injunction or temporary restraining order.

15 U.S.C. § 1116(a) (emphasis added), *as amended*, Trademark Modernization Act of 2020, The Consolidated Appropriations Act, 2021, Pub. L. 116-260, § 226, 134 Stat. 2208 (2020)). The District of Oregon recently applied this presumption in granting injunctive relief:

> Because Plaintiff has shown a likelihood of success of the merits on it motion for a temporary restraining order to enjoin Defendants' violation of 15 U.S.C. § 1125(a), Plaintiff is entitled to the benefit of the rebuttable presumption provided in § 1116(a). Anheuser-Busch has not rebutted that presumption. Accordingly, the Court finds that Plaintiff has shown a likelihood of irreparable injury.

Suzie's Brewery Co. v. Anheuser-Busch Co., No. 3:21-cv-178, 2021 WL 472915, at *12 (D. Ore. Feb. 9, 2021) (granting relief). Accordingly, here irreparable harm may be presumed.

Moreover, the harm at issue here is both "actual and imminent." *Regents of Univ. of Cal. v.*

ABC, Inc., 747 F.2d 511, 523-524 (9th Cir. 1984) (quotations omitted). Natera's false and misleading advertising causes multiple distinct types of irreparable harm: loss of customers and loss of reputation—injuries exacerbated by the nascent nature of this developing field. The potential loss of market share has long been considered an "irreparable" injury. *Am. Rena Int'l Corp. v. Sis-Jocye Int'l Co.*, 534 Fed. App'x. 633, 636 (9th Cir. 2013) (citing *Stuhlbarg Int'l Sales Co. v. John D. Brush & Co.*, 240 F.3d 832, 841 (9th Cir. 2001)); *Fla. Bus. for Free Enterprise v. City of Hollywood*, 648 F.2d 956, 958, fn. 2-3 (5th Cir. 1981); *Novartis*, 290 F.3d at 596 ("loss of market share" is irreparable); *Momento, Inc. v. Seccion Amarilla USA*, No. C 09-1223, 2009 WL 1974798 at *4 (N.D. Cal. July 8, 2009).

"Evidence of loss of control over business reputation and damage to goodwill can constitute irreparable harm." *2DIE4KOURT v. Hillair Cap. Mgmt., LLC*, 692 Fed. App'x. 366, 369 (9th Cir. 2017) (quotations omitted). *2DIE4KOURT* affirmed the grant of preliminary injunctive relief in a Lanham Act case involving the Kardashians, who claimed a former trademark licensee continued to use the sisters' marks after the agreement terminated. *Id.* Because the defendant released an unapproved line of cosmetics with the Kardashian mark, "the Kardashians likely will lose some measure of control over their business reputation in the absence of injunctive relief." *Id.* While defendant claimed the injunction would itself cause *it* irreparable harm by causing the termination of its business, the Ninth Circuit reasoned that "when the harm complained of results from a defendant's allegedly infringing conduct," a preliminary injunction nevertheless is proper. *Id.*

The potential injury here is, of course, far more severe. Guardant provides a life-extending cancer assay, and Natera's false advertising is intended to make physicians believe that Reveal is not safe or effective to use. *Osmose, Inc. v. Viance, LLC*—though involving treated wood rather than potentially life-saving medical technology—considered a comparable false advertising claim. 612 F.3d 1298 (11th Cir. 2010). There, defendant falsely claimed that the plaintiff's treated wood products were unsafe. "[O]n their face," the trial court reasoned, defendant's advertising claims "would likely cause irreparable harm," as the ads at issue "contained serious indictments of the safety of MCQ-treated products," and "would likely be remembered by consumers." *Id.* at 1320. Affirming the grant of injunctive relief, the Eleventh Circuit agreed that "[t]he inference that the

serious nature of the claims in the advertisements would irreparably harm [the plaintiff's] goodwill and market position is certainly reasonable." *Id.*; *see also United Tactical Sys., LLC v. Real Action Paintball, Inc.*, No. 3:14-cv-04050, 2014 WL 6788310, at *23 (N.D. Cal. Dec. 2, 2014) (loss of control over reputation and goodwill resulted in irreparable harm); *Maxim Integrated Prod., Inc. v. Quintana*, 654 F. Supp. 2d 1024, 1036 (N.D. Cal. 2009) (evidence plaintiff's mark was used by defendant in an interview and in a negative product review for defendant's product established plaintiff's loss of control over its business reputation and goodwill).

The fact that liquid biopsies represent a new technology makes Guardant's loss of customers and the damage to its reputation even more worthy of immediate injunctive relief. New technologies have different growth patterns than do their more mature counterparts, and are thus particularly vulnerable to disruptions during their early years. In *Illumina, Inc. v. Qiagen, N.V.*, 207 F. Supp. 3d 1081 (N.D. Cal. 2016), the court granted a preliminary injunction in a patent infringement action involving a similarly nascent industry developing DNA sequencing technology. *Id.* at 1094-95. Judge Alsup considered the irreparable harm the infringement would inflict *because* it took place at a pivotal moment during the infancy of the developing field:

> The market for DNA sequencing in clinical laboratories is expected to grow substantially in the near future, and Qiagen has a foothold in that market due to its other product lines. Now, as the doors to the market have swung open, Qiagen seeks to usurp Illumina's position in that market with pirated technology.

Id. at 1093. Thus, "if Qiagen were allowed to capture and define the market with pirated technology alongside its preexisting relationships and disruptive business model" during "this crucial inflection point in the development of the market for DNA sequencing equipment for clinical laboratories, Illumina would suffer irreparable harm." *Id.* Plaintiff's harm would "be compounded if Qiagen's products perform poorly," a "serious prospect" in that case. *Id.*

"[I]ntangible injuries, such as damage to ongoing recruitment efforts and goodwill, also qualify as irreparable harm." *Rent-A-Center, Inc. v. Canyon Television & Appliance Rental, Inc.*, 944 F.2d 597, 603 (9th Cir. 1991). By disrupting its product launch, Natera's false advertising has diminished Reveal's reputation and goodwill at a particularly critical juncture in the commercial life of Guardant's product, as there is always a significant education and persuasion process in

convincing medical professionals to use new products.

Accordingly, while irreparable injury is presumed, the evidence here plainly demonstrates that Guardant (and cancer patients who might benefit from Reveal) face a substantial risk of irreparable harm. Odegaard Decl. ¶¶ 18-19 & 29; *see also* Rich Decl. ¶ 37. Given the importance of the technology, the fast-approaching ASCO conference and the critical juncture in Reveal's marketing lifespan, the injury here is particularly severe.

D. THE BALANCE OF HARDSHIPS AND THE PUBLIC INTEREST FAVOR A TRO

The public interest is served by accurate advertisements—a principle that should hold particularly true in the context of diagnostic tools for life-threatening diseases. *See Am. Home Prods. Corp. v. Chelsea Labs., Inc.*, 572 F. Supp. 278, 286 (D.N.J. 1982) ("The Public Interest [element] is especially strong in prescription drug cases."); *see also Novartis*, 290 F.3d at 597 ("We agree with those district courts that have found that there is a strong public interest in the prevention of misleading advertisements, and this interest is particularly strong where over-the-counter drugs are concerned"); *POM Wonderful*, 2008 WL 4222045, at *16 ("There is a strong public interest in preventing false advertising of products in the marketplace.") (citations omitted); *see also Resource Lenders, Inc. v. Source Solutions, Inc.*, 404 F. Supp. 2d 1232, 1249-50 (E.D. Cal. 2005).

By contrast, there is no public interest in allowing false advertising. *See Suzie's Brewery*, 2021 WL 472915, at *12 ("A party does not have an equitable interest in disseminating a false advertisement.") A party can "assert no equitable interest in the perpetuation of an advertising campaign that is literally false." *Zeneca*, 1999 WL 509471, at *41. Thus, "when the potential harm to each party is weighed, a party can hardly claim to be harmed where it brought any and all difficulties occasioned by the issuance of an injunction upon itself." *Kos Pharm., Inc. v. Andrx Corp.*, 369 F.3d 700, 728 (3d Cir. 2004) (quotations omitted).

Because Natera will suffer no "harm" from an injunction requiring it to compete truthfully, and because Guardant faces significant harm if the false statements are allowed to continue, the balance of equities weighs heavily in favor of an injunction. *2DIE4KOURT*, 692 Fed. Appx. at 369; *see also Castrol Inc. v. Pennzoil Co.*, 799 F. Supp. 424, 440 (D.N.J. 1992) (a defendant in a Lanham Act case "can assert no equitable interest in the perpetuation of an advertising campaign that is

literally false."); *A.J. Canfield Co. v. Vess Beverages, Inc.*, 612 F. Supp. 1081, 1089 (N.D. Ill. 1985) (defendant is still "free to market its product truthfully and accurately.")

E. THE COURT SHOULD ISSUE A TEMPORARY RESTRAINING ORDER

Guardant presents all of the elements supporting a preliminary injunction, and the Court should exercise its discretion and grant a temporary restraining order. *Cf. TrafficSchool.com*, 653 F.3d at 829 ("Courts routinely grant permanent injunctions prohibiting deceptive advertising.") "The scope of an injunction is within the broad discretion of the district court." *Id.* Here, Guardant respectfully requests that the Court issue a targeted temporary restraining order, preventing Natera from continuing to claim that the use of Reveal will compromise patient care, as well as refraining from claiming that Signatera is superior when it is not.

BOND: This Court "'is afforded wide discretion in setting the amount of the bond," and "'the bond amount may be zero if there is no evidence the party will suffer damages from the injunction.'" *Cisco Sys*, 2020 WL 5199434, at *13 (quoting *Connecticut Gen. Life Ins. Co. v. New Images of Beverly Hills,* 321 F.3d 878, 882 (9th Cir. 2003)) (other citations omitted)). Here, in light of the clear evidence of Natera's Lanham Act violations, and the lack of any legitimate interest in continuing its false advertising, the Court should set the bond amount in this case at zero. *Id.* at *14.

IV. CONCLUSION

The Court should enter an Order temporarily restraining Natera from falsely advertising its tumor-dependent assay Signatera, including falsely describing Guardant's plasma-only Reveal assay as being non-validated, untested, inaccurate, insensitive, or inferior to Signatera.

Dated: June 2, 2021

NORTON ROSE FULBRIGHT US LLP
Saul Perloff

By: */s/Saul Perloff*
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